Scientific Abstract

Eradication of leukemia following MHC-matched allogeneic hematopoietic stem cell transplantation (HCT) is in part attributable to an immune-mediated graft-versus-leukemia (GVL) reaction mediated by donor T lymphocytes specific for minor histocompatibility (H) antigens of the recipient. Donor lymphocyte infusions have been used to treat patients with relapse of leukemia after HCT but are complicated by graft-versus-host disease (GVHD). Infusions of donor-derived $CD8^+$ cytotoxic T lymphocyte (CTL) clones specific for minor H antigens expressed on the recipient's leukemia cells, but only on a limited range of other recipient tissues, might provide for a selective GVL effect without inducing GVHD in patients with posttransplant relapse of leukemia. The proposed study will investigate the administration of donor-derived $CD8^+$ CTL clones specific for minor H antigens selectively expressed on recipient hematopoietic cells, including leukemic cells, but not recipient fibroblasts, to patients with relapse of acute leukemia or myelodysplastic syndrome (MDS) following MHC-identical allogeneic HCT. The first 3 infusions will consist of $CD8^+$ CTL clones that have been transduced with a retrovirus containing a hygromycin phosphotransferase – *Herpes simplex* virus thymidine kinase fusion gene (termed HyTK). Cells expressing the bifunctional HyTK fusion gene are hygromycin resistant but are also sensitive to ganciclovir or acyclovir. Modification of CTL to express the HyTK gene will allow their elimination *in vivo* if the minor H antigen recognized by the CTL clone is expressed on nonhematopoietic tissues *in vivo* and the infusions cause GVHD or other toxicity.